DRAFT ISSUE SUMMARY

TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES ADVISORY COMMITTEE MEETING

26 JUNE, 2002

ISSUE 2.

FDA Draft Guidance on Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Human Cells, Tissues, and Cellular and Tissue-Based Products

ISSUE

FDA published a draft guidance for comment in June 2002, entitled "Draft Guidance on Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Human Cells, Tissues, and Cellular and Tissue-Based Products." The guidance is modeled after a guidance regarding blood donation, entitled "Guidance for Industry: Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products" that was published as draft in August 2001 and finalized January 2002. Like the "blood" guidance, the "tissue" guidance contains interim recommendations for donor eligibility based upon CJD/vCJD risks, with explanations for these recommendations. We have used the same criteria (travel to or residence in BSE-affected countries for certain durations and during certain time periods) used in the "blood" guidance, because at the present time, we do not have information about risk reduction versus tissue supply. The "tissue" guidance differs from the final "blood" guidance in the following ways: (1) there is no two-phase implementation; (2) there is an exception for HLA-matched hematopoietic stem cell collection from donors who would otherwise be determined ineligible by the recommendations; and (3) there is a request to submit data to assess the impact of these recommendations on supply. The committee is asked to comment on the recommendations made in the draft guidance.

BACKGROUND AND DISCUSSION

At its January 2001, meeting, TSEAC members were asked to evaluate the risk of transmission of vCJD through the transplantation, implantation, infusion, or transfer of human cells, tissues and cellular and tissue-based products, to compare this risk to that of transfusion of blood and blood products, for which precautionary measures had already been adopted, and to recommend whether FDA should defer donors of these cells and tissues who have possibly been exposed to the BSE agent through residence in or travel to BSE countries. In addition, the committee was asked to consider how information

about residence/travel history could best be obtained, (e.g., interview) especially in the case of a cadaveric donor.

The committee heard information about the tissue distribution of infectivity in human and animal transmissible spongiform encephalopathies (TSE), CJD transmission by corneal transplantation, CJD risk among corneal donors, safety and supply of corneal transplants procured under legislative consent, risk of vCJD in recipients of hematopoietic stem cell (HSC) transplants, the impact on supply of HSC of deferring donors from the United Kingdom, tissue standards development in Canada, and the rate of donor deferral using a uniform donor history questionnaire developed by the American Association of Tissue Banks.

The TSEAC members unanimously agreed that there is a significant risk of transmission of vCJD from HCT/Ps that are transplanted, implanted, infused, or transferred, compared to the risk of transmission of vCJD by blood transfusion. Cells and tissues can be presumed to be at least as infectious as blood. Dura mater and cornea are the tissues with the greatest risk, and there is no reason to assume that the risk of vCJD is any less than that of sporadic CJD. Based upon the committee members' assessment of the risk of transmission of vCJD by cells and tissues, the majority believed that FDA should recommend donor deferral criteria for possible exposure to the BSE agent, but should provide an exception for HSC, with labeling. The committee did not give advice about particular countries, time periods, or duration of exposure, nor did they vote on a requirement for donor history interview. They did recommend that when a test for TSE-associated prion protein is validated, such a test should be used for tissue donors.

Based upon the committee's recommendations, FDA has published this draft guidance for comment. This draft guidance has been published prior to the finalization of the new Donor Suitabilty and Good Tissue Practice rules because the agency feels that the possibility of vCJD or CJD transmission through tissues is a potential public health threat that should be addressed now, though the draft guidance may need revision as new information is made available about testing technology, epidemiology, or the impact of this draft guidance on the HCT/P supply.

Recommendations for donor eligibility made in this draft guidance:

A potential HCT/P donor should be determined ineligible if the donor:

1) has been diagnosed with vCJD or any other form of CJD;

2) has been diagnosed with dementia or any degenerative or demyelinating disease of the central nervous system (CNS) or other neurological disease of unknown etiology; (HCT/Ps from donors with dementia confirmed by gross and microscopic examination of the brain to be caused by cerebrovascular accident, brain tumor, head trauma, or toxic/metabolic dementia and who are confirmed not to have evidence of TSE on microscopic examination of the brain may be acceptable based on an evaluation by the Medical Director.)

3) is at increased risk for CJD; (Donors are considered to have an increased risk for CJD if they have received a dura mater transplant, human pituitary-derived growth hormone, or have one or more blood relatives diagnosed with CJD.)

4) spent three months or more cumulatively in the U.K. (defined in Appendix of draft guidance) from the beginning of 1980 through the end of 1996;

5) is a current or former U.S. military member, civilian military employee, or dependent of a military member or civilian employee who resided at U.S. military bases in Northern Europe (Germany, U.K., Belgium, and the Netherlands) for 6 months or more from 1980 through 1990, or elsewhere in Europe (Greece, Turkey, Spain, Portugal, and Italy) for 6 months or more from 1980 through 1996;

6) lived cumulatively for 5 years or more in Europe from 1980 until the present (note this criterion includes time spent in the U.K. from 1980 through 1996);

7) received any transfusion of blood or blood components in the U.K. between 1980 and the present; or

8) has injected bovine insulin since 1980, unless you can confirm that the product was not manufactured after 1980 from cattle in the U.K.

HLA-matched hematopoietic stem cells (HSC) may be collected from a donor who would otherwise be determined to be ineligible by one or more of recommendations 3-8 above. Use of such HSC could be appropriate cells could be appropriate if necessary to achieve an appropriate match with a recipient and if the benefits of such use outweigh the risks. We will consider such use to be an urgent medical need.

REFERENCES:

TSEAC Transcripts, January 18-19, 2001:
http://www.fda.gov/ohrms/dockets/ac/cber01.htm.

Guidance for Industry: Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products, January 2002 (67 FR 2226, January 16, 2002) .
http://www.fda.gov/cber/gdlns/cjdvcjd.pdf. (***enclosed**)

Draft Guidance for Industry: Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Human Cells, Tissues and Cellular and Tissue-Based Products (HCT/Ps), June 2002
http://www.fda.gov/cber/guidelines.htm (***enclosed)**

Suitability of Donors of Human Cellular and Tissue-Based Products; Proposed Rule (64 FR 52696) September 30, 1999. http://www.fda.gov/cber/rules/suitdonor.pdf. (***enclosed—see topic 1)**

Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products; Inspection and Enforcement; Proposed Rule (66 FR 1508), January 6, 2001. http://www.fda.gov/cber/rules/gtp010801pr.htm. (***enclosed—see Topic 1)**

CHARGE

?? FDA asks the TSEAC to comment on the recommendations made in the draft guidance.

?? FDA asks the TSEAC to consider how information can be obtained about the effect of implementing these tissue donor deferral criteria on the tissue supply in the United States.